Remarks

Rejection Under 35 U.S.C. § 101

Claims 1-4 and 6-8, and 10 were rejected under 35 U.S.C. § 101, as being directed to non-statutory subject matter. Applicant respectfully traverses this rejection to the extent that it is applied to the claims as amended.

Claims 1 and 10 have been amended to recite that the organisms are selected from the group consisting of bacteria, plants, and yeast. Support for this amendment can be found on page 5, lines 18-21. The rejection should be overcome by this amendment.

Rejection Under 35 U.S.C. § 112, first paragraph (written description)

Claims 1-4 and 6-10 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicant respectfully traverses this rejection to the extent that it is applied to the claims as amended.

The written description requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or a disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

A 'representative number of species' means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus. See, e.g., *Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326-27. What constitutes a 'representative number' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

As demonstrated by the specification on page 6, lines 3-28 and Examples 1-3, and the publications submitted with the IDS and enclosed with the response filed February 2, 2005 (Leurs et al. *FEMS Microbiol. Lett.* 154(2): 337-345 (1997); Tong et al. *Appl. Environ. Microbiol.* 57(12):3541-3546 (1991); Yoshida et al. *Eur. J. Biochem.* 251:549-557 (1998) and op den Camp et al. *Plant Mol. Biol.* 35(3): 355-365 (1997)), one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus of aldehyde dehydrogenase and diol oxidoreductase in view of the species disclosed.

The specification and publications demonstrate that genes encoding aldehyde dehydrogenase and diol oxidoreductase could be obtained from a number of organisms, and sequence information for the genes were well known in the art, as of the priority date of this application, July 21, 2000. In addition, published amino acid and nucleotide sequence listings

for the various genes could be obtained from GenBank or the National Center for Biotechnology Information (NCBI) and actual DNA could be obtained from the authors of the publications or purchased from commercial suppliers, such as the American Type Culture Collection (ATCC).

In addition to those nucleic acid sequences defined as specific *aldH* and *dhaT* genes in the specification, the primer and/or oligonucleotide sequences used to hybridize to, and isolate, those sequences can be used to isolate genes encoding aldehyde deydrogenase and diol oxidoreductase from other organisms. For example, the specification states that the *aldH* gene was cloned by PCR from the *E. coli* genome **on the basis of its homology with other aldehyde dehydrogenases** using the oligonucleotide primers SEQ ID NO: 3 and SEQ ID NO: 4 (Example 1 and specifically, page 9, lines 29-30). The same oligonucleotide primers could be used to isolate genes encoding aldehyde dehydrogenase from other bacterial strains. The same process can also be used to isolate diol oxidoreductases from a number of organisms. The Examiner is referred to page 6, lines 3-28, which teaches that there are a variety of organisms from which the aldehyde dehydrogenase and diol oxidoreductase genes can be isolated. The methods in which one of ordinary skill in the art would use to isolate the claimed genes lie at the very heart of defining the structural nature of each gene. The structures of the claimed genes are clearly limited based, in part, on the requirement for them to be complementary to the primers and/or oligos disclosed, for example, in Example 1.

The Examiner alleges that the genus comprising aldehyde dehydrogenase and the genus comprising diol oxidoreductase comprises species that are structurally unrelated and utilize substrates unrelated to the diols recited in the claims. The claims have been amended to recite

that the enzymes expressed by the organisms can convert diols into hydroxyalkanaote monomers. Therefore, the claims are limited to those enzymes that can perform the recited function and do not include enzymes that cannot use diols as substrates.

Rejection Under 35 U.S.C. § 112, first paragraph (enablement)

Claims 1-4 and 6-10 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicant respectfully traverses this rejection to the extent that it is applied to the claims as amended.

As discussed above, the specification and the prior art disclose organisms that can be genetically engineered to produce PHAs (page 5, lines 18-21), diols that may be utilized to form the claimed hydroxyhexanoate monomers (page 9, lines 15-25), and organisms from which diol oxidoreductase and aldehyde dehydrogenase genes have been isolated and how to obtain these genes and enzymes (page 6, lines 2-28; Example 1). Methods for cloning genes encoding the enzyme are well known in the art and described in the application. For instance, Example 1 discusses a standard method for cloning the *aldH* gene from the *E. coli* genome using PCR. Similar methods can be used to clone aldehyde dehydrogenase and diol oxidoreductase genes from other organisms without undue experimentation. There is also sufficient direction and guidance given by the specification to construct plasmids and express the claimed genes (see Examples). In addition, the Applicants have provided working examples which demonstrate that one can use the claimed enzymes to engineer organisms to produce polyhydroxyalkanoates from diols, such as 1,4-butanediol (Examples 3, 4 and 7; 1,3-propanediol (Examples 5 and 6).

The Board of Patent Appeals and Interferences has held that claim language requiring operability may overcome a potential problem of a claim reading on a broad range of embodiments, many of which may be inoperative. *Ex parte* Mark, 12 USPQ2d 1904 (Bd. Pat. App. & Int'f 1989). The claims have been amended to limit the enzymes to those that can convert diols into hydroxyalkanaote monomers. Therefore, one of ordinary skill in the art would **not** select an enzyme that cannot perform this function.

In addition, there is no legal requirement that all of the enzymes within the scope of the claims convert the diols to their corresponding hydroxyalkanoate monomers for the enzymes to have the specified utility. In *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.* (1984), the Federal Circuit noted that "Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid ... [I]f the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid." *Atlas Powder Co. v. E. I. Du Pont de Nemours & Co.*, 750 F.2d 1569 (Fed. Cir.1984). It would only take routine experimentation, such as the screening methods described on page 7, line 24 to page 8, line 26, to identify other aldehyde dehydrogenases and diol oxidoreductases, for example, from the organisms recited on page 6, lines 3-28, that can convert the diols to their corresponding hydroxyalkanoates. Based on teachings in the specification and the state of the art, one of ordinary skill in the art would be able to select an appropriate aldehyde dehydrogenase or diol oxidoreductase for use in the claimed methods and systems.

It clear from the amount of direction or guidance presented in the specification, the presence of working examples, the state of the prior art, the relative skill in the art, and the breadth of the claims that one of ordinary skill in the art would be able to make and use the claimed genetically engineered organisms for the production of polyhydroxyalkanoates without undue experimentation.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 8 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

All of the claims have been amended to recite "polynucleotides" as suggested by the Examiner, because Applicants believe the term "genes" is encompassed by "polynucleotides". This amendment should overcome the rejection.

Allowance of claims 1-4 and 6-10, as amended, is respectfully solicited.

Respectfully submitted,

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Date: July 8, 2005

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